REMARKS

PRIORITY / SPECIFICATION

The Office action raises an issue about applicants' priority claim. Applicants claim priority to the GB application filed on 1 November 2002. This is stated on the Application Data Sheet as 01/11/2002 under the convention Day/Month/Year = 1/November/2002. The Office appears to have misunderstood this to be January 11, 2002 (Month/Day/Year). Applicants' PCT application was filed 3 November 2003, and validly claimed priority to 1 November 2002 since 1 November 2003 fell on a Saturday.

The Preliminary Amendment filed 29 April 2005 correctly refers to the filing date of the international application (November 3, 2003) stated as 03/11/2003 in the Application Data Sheet. The Preliminary Amendment filed 29 April 2005 correctly refers to the filing date of the GB priority application (November 1, 2002) stated as 01/11/2002 in the Application Data Sheet.

35 USC Section 112

Applicants request reconsideration of the objection to claims 44 and 63. Claim 44 has been amended to remove the "preferably" language. The "anodic bonding" in claim 63 is a term of the art in the field of semiconductor fabrication and, more particularly, micro-electromechanical devices. It is a technique for bonding glass to silicon. There are numerous references to it on the internet and elsewhere as, for example, in US Pat. 6,660,614 entitled METHOD FOR ANODICALLY BONDING GLASS AND SEMICONDUCTING MATERIAL TOGETHER. It would be well understood by the skilled person.

35 USC Section 103

Applicants respectfully request reconsideration of the rejection of the claims as obvious over the four-way combination of Goodey et al., Fogler, Costa et al, and Levesque et al.; and in Rejections # 2-6, further in view of additional references.

Claim 1 is directed to a microfabricated device for fragmenting nucleic acids and requires an inlet, an outlet, and a fragmentation cell having a top wall, bottom wall, and side walls which extend from the top wall to the bottom wall. The side walls taper inwardly to meet the inlet port. In claim 44, the outlet port comprises a constriction having a width in the range of from 1 to 100 μm.

First and foremost, a reference may only be relied upon in an obviousness rejection if the reference is analogous art to the application at issue. According to MPEP §2141.01(a):

> In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned. *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992).

Goodey et al. cannot fairly be relied on in an obviousness rejection since the reference is neither (1) in the field of applicants' endeavor, nor (2) reasonably pertinent to the particular problem with which the applicants were concerned. Applicants' field of endeavor as stated in claim 1 is a "device for fragmenting nucleic acids." As explained in applicants' paragraph 0002, nucleic acid fragmentation is, for example, chemically or physically breaking DNA or RNA into fragments for analyzing the nucleic acid or for genomic library projects.

In contrast to fragmentation of nucleic acids, the Goodey et al. reference is directed to a "Multianalyte Sensor Array Composed of Chemically Derivatized Polymeric Microspheres." As

explained in Goodey et al.'s Introduction, these arrays are being developed to assay "multifunctional fluids" (p. 2560, column 1), i.e., figure out what a particular fluid contains. It is related to electronically analyzing the taste and smell of fluids (p. 2560, column 2). It is evident from "Materials" (p. 2561, column 1), "Fabrication of the Microbead Arrays" (p. 2561, column 2), and "Fluid Package" (p. 2562, column 1) that the devices shown in Figures 1 and 2 relied on by the Office are packages containing a "taste chip" of special microbeads incorporated into silicon. Figures 1A and B show a "pit" in a Si chip for seating a microbead sensor. Figure B shows "an expanded view of the fluid delivery method and bead confinement strategy." A fluid to be analyzed is flowed over the microbead. The package with components of the fluid captured on the microbeads is then available for use in analyzing the fluid.

Packages for fluid analysis as in Goodey et al. are not in the field of fragmenting nucleic acids. So Goodey et al. cannot be relied on as in applicants' field.

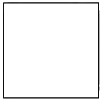
Nor can Goodey et al. be relied on as being "reasonably pertinent" to the problems with which applicants were concerned. The problems faced by applicants related to breaking RNA and/or DNA under mechanical force (see 0013). Goodey et al.'s capturing multi-component fluids in a manner suitable for electronic taste/smell analysis has nothing to do with fragmenting nucleic acids, and therefore is in no way "reasonably pertinent" to applicants' problem.

And in contrast to fragmenting nucleic acids, the second piece of prior art relied on by the Office -- Fogler's Figure 6-16 -- is a fluidized continuous-stirred tank reactor (CSTR) described on page 272 as "a catalytic or fluid-solid reactor." This is a reactor for obtaining "perfect mixing behavior" to facilitate a catalyzed chemical reaction. Fluid-solid chemical reactions and CSTRs are not in applicants' field of fragmenting nucleic acids. And Fogler's problems of, e.g., achieving the

proper liquid-solid mixing and interface dynamics are in no way pertinent to applicants' problem of breaking up nucleic acids. Breaking up nucleic acids is not a liquid + solid mixing operating.

The irrelevance of the Fogler reference is underscored by the fact applicants' device is *micro*fabricated, whereas CSTRs -- obviously not suited for nucleic acid fragmentation -- are generally large, as shown in this photo from Wikipedia:

Fogler refers to a "Berty reactor," -- also not suitable for nucleic acid fragmentation -- but even a *micro*-Berty reactor has a 4-inch dimension:



Hannoun et al., "Mixing Characteristics of a Micro-Berty Catalytic Reactor" Ind. Eng. Chem Res. 1992, 37, 1288-1292.

In view of the foregoing, all of the rejections should be withdrawn because neither Goodey et al. nor Fogler are analogous art.

The rejections should also be withdrawn because even if the Goodey et al. and Fogler references were analogous art, they are so unrelated to each other -- Goodey et al.'s isolating a fluid sample for electronic taste and smell analysis *versus* Fogler's chemical reaction vessel -- that there is absolutely no *reason* one skilled in the art would incorporate aspects from Fogler's reactor into Goodey et al.'s microbead sample-chip package.

And the rejections should also be withdrawn because there is no reason for one skilled in the art to take Fogler's "taper-toward-the-inlet-port" feature and incorporate it into Goodey et al.'s sample package. The Office asserts on page 9 of the Office action that a reason is that Fogler's taper provides better mixing. But there is no discussion of why any such mixing would be desirable in the Goodey et al. device. Goodey et al.'s taper shown in Fig. 2B from wider at the inlet to narrower at the outlet is part if their "bead confinement strategy." Goodey et al. are confining a bead in this depression, and then flowing a fluid over the top of it. There is no desire, need, or use for "better mixing"; so there is no reason to make the proposed modification. Turbulence as shown in Fogler would seem to

undesirably unseat Goodey et al.'s bead. And if there were tapering toward the inlet, it is unclear how one would seat the bead, at least if the inlet were any scale imaginably analogous to the scale of the outlet shown in Goodey et al.'s Fig. 2B.

Applicants therefore respectfully request withdrawal of all the rejections on the basis that

a) the two primary references are not analogous to the claimed invention;

b) the two primary references are wholly unrelated to each other, so there is no basis to combine them; and

c) the reason Fogler tapers toward an inlet has no relevance to either Goodey et al.'s microbead sampling array package or to applicants' nucleic acid fragmentation; so there is no legitimate reason to make the proposed modification.

In addition to the foregoing, applicants note the following:

The third reference Levesque et al. is related to "The Elongation and Orientation of Cultured Endothelial Cells in Response to Shear Stress"; which has absolutely nothing to do with microbead sampling packages (Goodey et al.) or chemical reaction vessels (Fogler).

Lavesque et al. channel flow configuration is concerned with hemodynamics, and employ parallel plates for steady, uniform, laminar flow (see p. 342, column 1, under "Parallel Plate, Channel Flow Device"); which is wholly distinct from applicants' gradual constriction to achieve fragmentation by shearing.

The Costa et al. reference is cited for the proposition that Lavesque et al.'s shearing principles apply to oligonucleotides. Whether or not this is the case, the Costa et al. reference does not cure the many other deficiencies of the proposed combination.

Inasmuch as all of rejections #1-6 rely on the same combination of these four references, Applicants respectfully

request withdrawal of all the rejections.

CONCLUSION

Applicants request issuance of a Notice of Allowability for all pending claims.

Respectfully submitted,

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